Rejections Under 35 U.S.C. § 112, First Paragraph

Claims 38-47 are rejected as the specification, while enabling for a method for protecting a bone marrow cell by administering a polypeptide consisting of SEQ ID NO: 6, is allegedly not enabling for administering a polypeptide *comprising* SEQID NO: 6.

Applicants thank the Examiner for noting that the specification is enabling for methods of protecting a bone marrow cell by administering a polypeptide consisting of SEQ ID NO: 6. However, Applicants submit that polypeptides comprising SEQ ID NO: 6, and methods of using these polypeptides to protect bone marrow cells, are fully enabled by the specification.

The specification clearly describes fusion proteins including SEQ ID NO: 6 and a carrier protein (e.g. see page 14, lines 20-25). For example, these fusion proteins are described that include maltose binding protein (MBP), glutathione-S-transferase, or six histidine residues. In addition, two polypeptides comprising SEQ ID NO: 6, namely SEQ ID NO: 4 and SEQ ID NO: 5, and their use, are disclosed in the specification (e.g. see page 13, line 28 to page 14, line 3). Specific examples of the actual preparation of fusion proteins including SEQ ID NO: 6 are further provided in the Examples section of the specification. For example, production of a fusion protein including SEQ ID NO: 6 and maltose binding protein (MBP) is disclosed in the specification, including cloning and purification (e.g. see the specification on page 39, lines 1-15).

The specification discloses that the MBP-SEQ ID NO: 6 fusion polypeptide was tested for its ability to stimulate bone marrow cells. The specification clearly describes that MBP-SEQ ID NO: 6, but not a denatured control, stimulates bone marrow cells. The specification further describes that the use of MBP-SEQ ID NO: 6 fusion protein includes the active site for required for activity (see Example 6 of the specification, on page 39, line 1to page 40, line 4). The specification also describes that MBP fusion proteins are effective when used *in vivo* to protect hematopoietic stem cells from toxicity (see Example 4 of the specification, at page 31, line 12 to page 32, line 25). Specifically, the specification discloses that examination of the femoral bone marrow of mice treated with MBP alone prior to irradiation had reduced cellularity, while mice treated with a fusion protein including both SEQ ID NO: 6 and MBP had increased cellularity (see page 32, lines 1-6). In addition, *in vivo* protection of hematopoietic stem cells from chemotherapy induced toxicity using a polypeptide including SEQ ID NO: 6 is described in the

specification on page 27, line 13 to page 30, line 20.

Thus, not only are a number of proteins comprising SEQ ID NO: 6 described sufficiently for one of skill in the art, a specific example describing the production of an exemplary fusion protein (MBP) is provided in the specification, and actual experimental results obtained using a polypeptide comprising SEQ ID NO: 6 are disclosed. Thus, the specification is clearly enabling for polypeptides comprising SEQ ID NO: 6, as well as for methods for protecting a bone marrow cell using a polypeptide comprising SEQ ID NO: 6.

Applicants respectfully disagree with the assertion in the Office action that "protein chemistry is one of the most unpredictable areas of biotechnology." The production of polypeptides of a known sequence is routine in any molecular biology lab. Molecular techniques, such as expression vectors, and the expression of cloned polypeptides, and the expression of fusion proteins, are in routinely use in a myriad of molecular biology laboratories throughout the United States (and throughout the world). In fact, polypeptides, vectors for the production of fusion protein, and cells for producing polypeptides and fusion proteins, can be ordered from many commercial laboratories.

In the present case, the polypeptides of use must include the sequence set forth as SEQ ID NO: 6. SEQ ID NO: 6 is an eighteen amino acid long polypeptide that is demonstrated in the present application to include the active site of vasostatin for the protection of bone marrow cells. However, the Office action appears to require identification of active amino acid residues within this eighteen amino acid sequence to enable claims to the use of polypeptides including SEQ ID NO: 6.

The Office action further gives an example wherein aspartic acid at position 47 of TGF is replaced with alanine or asparagine, and a non-functional polypeptide is produced. This scenario simply does not apply here. As claimed, the polypeptide must include SEQ ID NO: 6; any alteration, truncation, substitution of SEQ ID NO: 6 is not encompassed by the pending claims, as this polypeptide would not comprise SEQ ID NO: 6. Therefore, applicants fail to understand how they can be compelled to disclose which residues in an eighteen amino acid polypeptide are essential for function to enable claims 38-46 as pending, nor can they be compelled to describe functional variants.

Applicants have clearly provided a complete description of the polypeptides of use, set forth exemplary polypeptides, and disclosed actual production of polypeptides comprising SEQ

ID NO: 6 and described results from actual testing of these polypeptides documenting that they protect bone marrow cells from toxicity induced by chemotherapy and radiation. Thus, applicants submit that claims 38-46 are fully enabled by the specification.

Reconsideration and withdrawal of the rejection is respectfully requested.

Claims 38-47 are rejected as allegedly the specification does not contain sufficient written description for polypeptides comprising SEQ ID NO: 6, with an additional amino acid sequence than SEQ ID NO: 6. Applicants respectfully disagree with this assertion.

As discussed above, the specification clearly describes fusion proteins including SEQ ID NO: 6 and a carrier protein (e.g. see page 14, lines 20-25). For example, these fusion proteins are described as including maltose binding protein (MBP), glutathione-S-transferase, or six histidine residues. Moreover, specific examples of the actual preparation of fusion proteins including SEQ ID NO: 6 are provided in the specification. For example, production of a fusion protein including SEQ ID NO: 6 and maltose binding protein (MBP) is disclosed, including cloning and purification (e.g. see the specification on page 39, lines 1-15). Polypeptides including SEQ ID NO: 6 are further set forth as SEQ ID NO: 4 and SEQ ID NO: 5.

As described above, the specification discloses the use of the MBP-SEQ ID NO: 6 fusion polypeptide to stimulate bone marrow cells. In addition, the specification discloses results obtained using an MBP-SEQ ID NO: 6 fusion polypeptide on bone marrow cells, and describes that MBP-SEQ ID NO: 6 stimulates bone marrow cells. Moreover the specification further discloses that MBP fusion proteins are effective in vivo to protect hematopoietic stem cells from toxicity (see Example 4 of the specification, at page 31, line 12 to page 32, line 25) induced by radiation (see page 32, lines 1-6). In addition, the *in vivo* protection of hematopoietic stem cells from chemotherapy induced toxicity using a polypeptide including SEQ ID NO: 6 is described in the specification on page 27, line 13 to page 30, line 20. Clearly, in order to produce the fusion proteins described in the specification, and to produce the experimental data disclosed, the Applicants had to be in full possession of the invention at the time the application was filed.

Thus, as a number of proteins comprising SEQ ID NO: 6 are described sufficiently for one of skill in the art to produce these proteins, and as a specific example describing the production of an exemplary fusion protein (MBP) is provided in the specification, and a actual experimental results obtained using a polypeptide comprising SEQ ID NO: 6 are disclosed.

Applicants submit, therefore, that the specification provides sufficient written description for claims 38-46.

Reconsideration and withdrawal of the rejection is respectfully requested.

CONCLUSION

It is respectfully submitted that claims 38-46 are in condition for allowance, which action is requested. If any matters remain to be discussed before a Notice of Allowance is issued, the Examiner, or the Examiner's supervisor, is requested to contact the undersigned at the telephone number listed below.

Respectfully submitted,

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